
Combined Chemical Treatment Enables Oct4-Induced Reprogramming from Mouse Embryonic Fibroblasts.

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Public Summary:

It has been established that exogenous expression of four transcription factors (Oct4, Klf4, Sox2 and c-Myc) can reprogram mammalian somatic cells to pluripotent states. Further studies demonstrated that such induced pluripotent stem cells (iPSCs) could be generated with fewer exogenous transcription factors, facilitated by endogenous expression of reprogramming factors and/or synthetic small molecules. Here, we reported identification of a new small molecule, a protein arginine methyltransferase (PRMT) inhibitor AMI-5, which enabled Oct4-induced reprogramming of MEFs in combination with TGF-beta inhibitor A-83-01. The Oct4-induced iPSCs were shown similar to mouse embryonic stem cells (mESCs) with respect to typical pluripotency criteria. More importantly, they were shown to give rise to live-born pups through tetraploid complementation assays, demonstrating the high quality of full reprogramming induced by this condition. Furthermore, this study suggests that regulation of protein arginine methylation might be involved in the reprogramming process.

Scientific Abstract:

It has been established that exogenous expression of four transcription factors (Oct4, Klf4, Sox2 and c-Myc) can reprogram mammalian somatic cells to pluripotent states. Further studies demonstrated that such induced pluripotent stem cells (iPSCs) could be generated with fewer exogenous transcription factors, facilitated by endogenous expression of reprogramming factors and/or synthetic small molecules. Here, we reported identification of a new small molecule, a protein arginine methyltransferase (PRMT) inhibitor AMI-5, which enabled Oct4-induced reprogramming of MEFs in combination with TGF-beta inhibitor A-83-01. The Oct4-induced iPSCs were shown similar to mouse embryonic stem cells (mESCs) with respect to typical pluripotency criteria. More importantly, they were shown to give rise to live-born pups through tetraploid complementation assays, demonstrating the high quality of full reprogramming induced by this condition. Furthermore, this study suggests that regulation of protein arginine methylation might be involved in the reprogramming process.

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